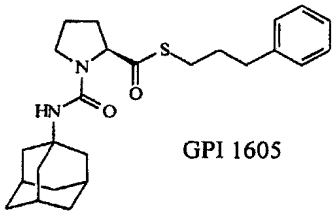
DETAILED DESCRIPTION OF THE INVENTION

Definitions

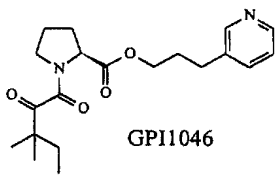
"Eye" refers to the anatomical structure responsible for vision in humans and other animals, and encompasses the following anatomical structures, without limitation: lens, vitreous body, ciliary body, posterior chamber, anterior chamber, pupil, cornea, iris, canal of Schlemm, zonules of Zinn, limbus, conjunctiva, choroid, retina, central vessels of the retina, optic nerve, fovea centralis, macula lutea, and sclera.

"GPI 1605" refers a compound of formula



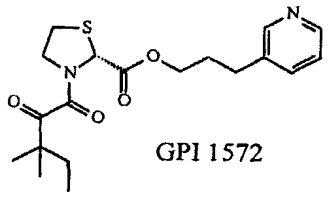
GPI 1605

"GPI 1046" refers to 3-(3-pyridyl)-1-propyl (2s)-1- (3,3-dimethyl-1,2-dioxopentyl) -2- pyrrolidine-carboxylate, a compound of formula



GPI1046

In a preferred embodiment of the compounds of formula II, the heterocyclic ester or amide is the compound GPI 1572, of the formula



GPI 1572

In a particularly preferred embodiment of formula II compounds:

A is CH_2;

B is CH_2 or S;

C is CH_2 or NH;

R_1 is selected from the group consisting of 3-phenylpropyl and 3-(3-pyridyl)propyl; and

R_2 is selected from the group consisting of 1,1-dimethylpropyl, cyclohexyl, and tert-butyl.

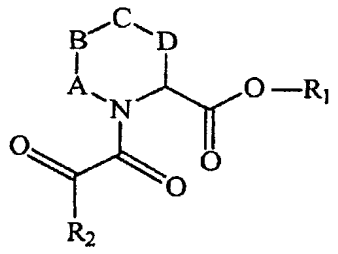
Specific examples of this embodiment are presented in TABLE I.

TABLE I

No.	A	B	C	R_1	R_2
1	CH_2	S	CH_2	3-phenylpropyl	1,1-dimethylpropyl
2	CH_2	S	CH_2	3-(3-pyridyl)propyl	1,1-dimethylpropyl
3	CH_2	S	CH_2	3-phenylpropyl	cyclohexyl
4	CH_2	S	CH_2	3-phenylpropyl	tert-butyl
5	CH_2	CH_2	NH	3-phenylpropyl	1,1-dimethylpropyl
6	CH_2	CH_2	NH	3-phenylpropyl	cyclohexyl
7	CH_2	CH_2	NH	3-phenylpropyl	tert-butyl

FORMULA III

The heterocyclic ester or amide may also be a compound of formula III



III

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A, B, C and D are independently CH_2, O, S, SO, SO_2, NH or NR_1;

R_1 is C_1-C_5 straight or branched chain alkyl or C_2-C_5 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$ and C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$;

n is 1 or 2;

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, or Ar_1; and

Ar_1 is an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted with one

Efficacy of representative compounds from different immunophilin ligand series in protecting retinal ganglion cell axons from degeneration following optic nerve transection

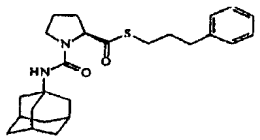
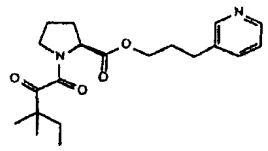
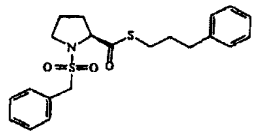
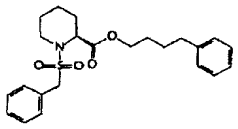
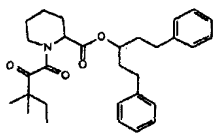
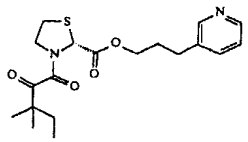
Compound	Structure	Comments	RT97+RGC axon density 14 days after ON transection (% ON axons rescued)
B		Adamantyl Thioester of urea Ki rotamase = 149 nM Clearance=? µl/min	100.0% ±5.2% SEM
A GPI 1046		Ester Ki rotamase = 7.5nM Clearance=63.8 µl/min	60.5% ±3.9 SEM
C		Sulfonamide Ki rotamase = 107nM Clearance= 31.1µl/min	60.4% ±3.1 % SEM
D		Pipecolic sulfonamide Ki rotamase= nM Clearance= µl/min	58.4% ±6.4% SEM
E		Ester of pipecolic acid Ki rotamase = 20 nM Clearance = 41.8 µl/min	56.6% ±9.4% SEM
F		Proline heterocycle Analog of GPI 1046 Ki rotamase = 272 nM Clearance=? µl/min	55.1% ±5.9% SEM

TABLE V